

WE CLAIM:

1. A method for the treatment or prevention of a condition requiring a reduction in the activity of a CYP2A enzyme in an individual in need thereof comprising administering an effective amount of one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; (iii) substances which delete all or a portion of the gene encoding CYP2A.
2. A method according to claim 1 wherein said CYP2A enzyme is CYP2A6.
3. A method according to claim 1 or 2 wherein said condition is smoking and inhibition of the CYP2A enzyme inhibits the conversion of nicotine to cotinine.
4. A method according to any one of claims 1 to 3, further comprising administering nicotine to said individual contemporaneously with said one or more substance.
5. A method according to claim 4, wherein said nicotine is formulated for oral administration.
6. A method according to claim 5, wherein said one or more substances and said nicotine are formulated in a single composition.
7. A method according to any one of claims 1 to 6, wherein said substances which inhibit CYP2A6 are selected from methoxsalen, psoralen, tranylcypromine, pilocarpine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline and pargyline.
8. A method according to any one of claims 1 to 6, wherein said substances which inhibit CYP2A6 are selected from methoxsalen, coumarin and tranylcypromine.
9. A method according to claim 8, wherein methoxsalen is administered in an amount from 0.1 mg to 50 mg; coumarin is administered in an amount from 1 mg to 1000 mg; or tranylcypromine is administered in an amount from 0.1 mg to 80 mg.
10. A method according to any one of claims 1-6, wherein said substances which inhibit CYP2A6 are natural products.

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11. A method according to claim 10, wherein said natural products are selected from Hypericum, Cichorium intybus, Bougainvillea spectabilis, and extracts thereof.

12. A method according to any one of claims 1 to 11, further comprising administering an inhibitor of CYP2B6 to said individual contemporaneously with said one or more substance.

13. A method according to claim 1 or 2 wherein said condition is cancer and inhibition of the CYP2A enzyme inhibits the metabolism of a procarcinogen to a carcinogen.

14. A method according to claim 13, wherein said procarcinogen is a N-nitrosodialkylamine selected from the group consisting N-nitrosodiethylamine, N-nitrosodimethylamine, and 4-methylnitrosamino)-1-3-pyridyl)-1-butanone.

15. The method of any one of claims 1-14, wherein said individual is suffering from a condition selected from (i) addiction to tobacco, (ii) risk of developing an addiction to tobacco, (iii) risk of developing a smoking associated cancer, and (iv) exposure to one or more compounds which are converted to carcinogens by CYP2A6.

16. A composition for use in the treatment or prevention of a condition requiring a reduction in the activity of a CYP2A enzyme comprising an effective amount of one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; (iii) substances which delete all or a portion of the gene encoding CYP2A in admixture with a suitable diluent or carrier.

17. A composition according to claim 15 wherein said CYP2A enzyme is CYP2A6.

18. A composition according to claim 16 or 17 wherein said condition is smoking and inhibition of the CYP2A enzyme inhibits the conversion of nicotine to cotinine.

19. A composition according to claim 18, wherein said composition further comprises nicotine.

20. A composition according to any one of claims 16-19, wherein said substance which inhibits CYP2A is a natural product.

21. A composition according to any one of claims 16-19, wherein said substance which inhibits CYP2A is selected from methoxsalen, psoralen, tranlylcypromine, pilocarpine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline and pargyline.

5 22. A method for enhancing the effectiveness of a nicotine replacement therapy comprising contemporaneously administering to an individual in need (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; (iii) substances which delete all or a portion of the gene encoding CYP2A.

10 CYP2A.

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23. A method according to claim 27 wherein said substance inhibits CYP2A6 and is selected from methoxsalen, psoralen, tranlylcypromine, pilocarpine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline and pargyline.

24. A kit for use in the method of claim 22 or 23 comprising (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; (iii) substances which delete all or a portion of the gene encoding CYP2A.

15 CYP2A.

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25. A method for determining the risk of an individual becoming a smoker comprising determining the genotype or phenotype of a CYP2A allele in the individual wherein the presence of a mutant allele is predictive of a decreased risk of smoking.

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26. A method for determining the risk of an individual for developing cancer comprising determining the genotype or phenotype of a CYP2A allele in the individual wherein the presence of a mutant allele is predictive of a decreased risk of developing cancer.

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27. A method according to claims 25 or 26, wherein said CYP2A enzyme is CYP2A6.

28. A method according to any one of claims 25 to 27, comprising analyzing a DNA-containing bodily sample from the individual for the presence of a mutant allele of human cytochrome P450 isozyme CYP2A6.

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29. A method according to claim 28, wherein said DNA-containing bodily sample is selected from a bodily fluid, a blood sample, blood plasma, and peripheral leukocytes.

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5 30. A kit for use in the method of any one of claims 25-29, comprising means to identify a mutant allele of CYP2A6.

31. The method of claim 25-29, the method comprising the steps of: administering a dose of a CYP2A6 substrate to the individual and determining in a bodily sample from the individual the level of said CYP2A6 substrate or a metabolite of said CYP2A6 substrate.

10 32. A kit for use in the method of claim 31, comprising a CYP2A6 substrate and means for quantifying said CYP2A6 substrate or a metabolite of said CYP2A6 substrate.

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